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| 10/690,618 | 10/23/2003 | Jon Wulff Petersen | 4528-0114P | 5915 |
| 2292 7590 05/07/2007 BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747 | | | EXAMINER OLSEN, KAJ K | |
| | | | ART UNIT 1753 | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary

Application No.

10/690,618

Applicant(s)

PETERSEN ET AL.

Examiner

Kaj K. Olsen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 10-23-03, 6-24-04, 8-27-04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____.

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities: the first paragraph of the specification should be amended to state that application 09/676,814 has matured into US Patent 6,682,649.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
4. In claim 1, line 2, the limitation "the first surface part" lacks antecedent basis. In line 5 of this claim, the limitation "the second surface part" also lacks antecedent basis. Moreover, the whole recitation of this second surface part is confusing because applicant never particularly claims that the substrate has a second surface part, but merely indirectly defines it as being something the specified passage goes through. The claims should be amended to clearly define that the substrate comprises a first surface part and a second surface part.
5. In claim 1, line 17, "the outer surface" presumably should be --an outer surface--.

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6. In claim 1, line 18, it is unclear if the “a first surface part” is referring to the previous “the first surface part” or some other element of the substrate.

7. Claims 1-3 define a series of elements and it is unclear what all these various elements correspond to elements in the disclosure or how these various elements cooperate with each other. In particular, applicant defines in these claims that the plane substrate comprises the following 12 elements: first surface part, second surface part, first side, second side, first substrate thickness, second substrate thickness, first substrate component, second substrate component, first side of the first substrate component, opposite side of the first substrate component, first side of the second substrate component, and opposite side of the second substrate component. The examiner notes that most of these claim terms listed above do not correspond to language utilized in the specification to define the invention rendering it unclear what each element of the claims is referring to. Moreover, applicant has not defined the correlation between these various elements clearly enough to render it clear how these various elements cooperate to define the invention. The examiner has made various attempts to sketch out what each of these various claimed elements are referring to and has not been able to successfully account for what all of these defined elements are referring to. What do the first and second substrate components of claim 3 refer to? Elements 12 and 17 of fig. 2C, the lower portion of element 12 and 13 of fig. 2B? Are the first and second substrate thicknesses of claim 2 referring to the thicknesses of the first and second substrate components of claim 3? If so, then it is why the applicant specifies a thickness for a component before they actually define the presence of the element itself. Moreover, if this were true, then why does claim 3 state that the first faces of the first and second substrates correspond to the first and second sides of claim 2

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(and hence the first and second substrate thicknesses couldn't correspond to the first and second substrate components). If not, then what is the relationship between the thicknesses of claim 2 and the components of claim 3. The examiner requests the applicant clarify these claims and/or explain how the various defined elements of the claims correspond to defined elements in the originally filed disclosure.

8. Claims 24-26 are confusing for the same reasons that claims 1-3 were above.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-15 and 17-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/31503 (hereafter "WO '503") in view of Nisch et al (USP 6,315,940), Rubinsky et al (USP 6,300,108) or Kostyuk et al (Nature, 257, pp. 691-693, October 1975).

12. WO '503 discloses an assembly comprising a plane substrate 1 having a plurality of sites adapted to hold an ion-channel containing structure (i.e. a cell) each of which have a passage 3 dimensioned to hold the ion-channel containing structure and form a high resistance seal between the ion-channel containing structure and the substrate along the passage. See fig. 3 and p. 12, ll. 12-27 for a discussion of the individual sites and claim 11 for a discussion of the plurality of sites. WO '503 further discloses a plurality of measuring electrodes 9 and reference electrodes 6 each associated with each respective site. Each of the sites is adapted to provide a high electrical resistance seal between an area of contact with an outer surface of a ion channel containing structure and the first surface part of the substrate whereby a current flowing between the reference and measuring electrodes and through the ion channel containing structure can be determined and monitored. See p. 12, ll. 12-27 and p. 15, l. 15 through p. 16, l. 4. Figures 3 and 4 of WO '503 also show the electrodes being integrated with the assembly. WO '503 does not explicitly recite the presence of a plurality of flow channels created in the substrate for delivering liquids to the sites. However, WO '503 does suggest that the compartments of its substrate can be connected to conventional flow systems for delivering fluids to the various compartments. Nisch, Rubinsky, and Kostyuk all teach how to integrate flow channels to electrophysiological substrates. In particular, Nisch teaches the presence of flow channels 23 etched into the substrate to provide fluid and electrical contact for the cells. See fig. 1A, 1B and col. 6, l. 64 through col. 7, l. 20. Rubinsky also teaches the presence of channels (13 and the inlet and outlet for 13) for delivering needed fluid to the lower compartment and cell to be treated. See fig. 1 and 2 and col. 6, ll. 49-65. Kostyuk also discloses the use of a flow channel beneath an electrophysiological site for controlling fluid content for the voltage clamping experiment. See fig. 1. It would have

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been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of any of Nisch, Rubinsky, or Kostyuk for the device of WO '503 so as to conveniently interface fluid inlet and outlet to the lower compartments of cell assays.

13. With respect to the remainder of the structural limitations of claims 1-3, it is noted that the examiner had trouble deciphering how the various claimed elements read on the instant invention. Because the plurality of sites structure taught by WO '503 is very similar to the structure of the instant invention (compare fig. 4A of the instant invention to fig. 3 of WO '502), and because the flow channel structures of Nisch, Rubinsky, and Kostyuk are very similar to the flow channels of the instant invention (compare the figure referred to above from Nisch, Rubinsky, and Kostyuk to fig. 4A of the instant invention), the examiner will tentatively presume that the set forth structure of WO '503 in view of any of Nisch, Rubinsky, or Kostyuk would meet these limitations even though it is unclear what these limitations are precisely setting forth (see 112 rejection above).

14. With respect to the silicon/silica substrate, see p. 12, ll. 22 and 23 of WO '503.

15. With respect to the presence of at least 9 sites, WO '503 didn't explicitly disclose a number of sites. However, it would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize at least 9 sites such that a large number of parallel ion channel analyses could be performed at the same time for greater information throughput. In addition, Nisch discloses the use of at least 9 measuring sites as well. See fig. 4.

16. With respect to the use of silver/silver halide electrodes. See WO '503, p. 20, ll. 18-22. See also Kostyuk, p. 692, where Ag/AgCl electrodes are utilized for both the measuring and reference electrodes.

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17. With respect to the hydrophobic material, see p. 13, ll. 19-21.

18. With respect to the use of funnel shaped wells, see fig. 1 and 3 and p. 21, l. 4 of WO '503. See also Nisch, fig. 3, 5, and 6.

19. With respect to the process that the wells are to be formed, the determination of patentability for the claim is based on the product itself. Because the product of the claim is identical to the invention of WO '503 in view of Nisch, Rubinsky, or Kostyuk, the process from which it was made is the same as or obvious over the process utilized by WO'503 in view of Nisch, Rubinsky, or Kostyuk (see *In re Thorpe*, 777 F.2d 695, 698).

20. With respect to the reference electrode being positioned on a side surface of the well, electrode 9 of fig. 3 of WO '503 is along a side surface of the well. With respect to this electrode being a reference electrode, the term "reference electrode" merely identifies how one intends to utilize said electrode and doesn't further define any inherent structure for the electrode (especially when applicant utilizes Ag/AgCl for both the measuring and reference electrodes. Hence, electrode 9 of fig. 3 would read on the defined reference electrode.

21. With respect to the generation of an amplified signal, fig. 1 of Kostyuk shows a high gain amplifier connected to the measuring electrodes.

22. With respect to the specified mean for connecting, both Rubinsky (col. 12, l. 49 through col. 13, l. 5) and Kostyuk (p. 692) teach the use of pressure differentials for creating a suction.

23. With respect to the method claims (those limitations not covered above), WO '503 also measures the resistance of its voltage clamps (p. 28, ll. 5-12), which WO '503 earlier disclosed is arrived at by a measurement of voltage and current and an application of Ohm's law. See p. 15, ll. 8-14. Hence, WO '503 already discloses applying a first electric potential difference and

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monitoring a first current flow in order to measure the strength of the electric seal. With respect to this applied potential difference being successive, fig. 9 shows a continuous (i.e. successive) monitoring of current until a suitable current level is measured. See the description of fig. 9 on p. 11. With respect to comparing this first current to a predetermined threshold current, because WO '503 already recognized what it deemed to be acceptable levels of current leakage (p. 15, ll. 15-19), one possessing ordinary skill in the art would have been motivated to only deem a seal to be acceptable provided it arrives a first current that is below or at a predetermined threshold current (as fig. 9 appears to be indicating). With respect to measuring a third current, once the seal of WO '503 is established, WO '503 shows in fig. 12 the analysis that proceeds. See the description of fig. 12 on p. 11.

24. With respect to the pore former, see WO '503, p. 23, ll. 5-9.

25. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO '503 in view of any of Nisch, Rubinsky, or Kostyuk as set forth for claim 15 above, and in further view of Knoll et al (USP 5,393,401).

26. The references set forth all the limitations of the claim, but does not explicitly identify the use of a 54.7° slope for the well openings (although fig. 1 of WO '503 appears to be substantially close to 54.7°). However, Knoll teaches that said angle is the conventional result of an anisotropic etching of a single crystal Si wafer. Said angle provides a continuous (111) crystal plane thereby improving the stability of the wafer surface (col. 2, line 60 through col. 3, line 8). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Knoll for the device of WO '503 in order to provide stable crystal surfaces along the etched out substrate well.

Double Patenting

27. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

28. Claims 1-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,682,649 in view of any of Nisch, Rubinsky, or Kostyuk.

29. The claims of the instant invention substantially overlap the claims of the patent. In particular, claim 1 of the patent appears to substantially comprise limitations from claims 1, 15, and 23 of the instant invention. Claim 24 of the patent appears to substantially comprise limitations 24 and 23 of the instant invention. Hence, most of claims 1 and 24 of the instant invention fully encompass the claims of the patent. Although the claims of the patent do not explicitly recite the presence of flow channels, the various teachings of Nisch, Rubinsky, and Kostyuk all rendered obvious the addition of flow channels to the substrate for the delivery of

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fluid to the measurement sites (see detailed discussion above). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teachings of any of Nisch, Rubinsky, or Kostyuk for the claimed invention of the patent so that fluid can be easily delivered to the measurement sites. With respect to the various dependent claims of the instant invention, these limitations all appear to have claim limitations in the patent and also fully encompass the claims of the patent.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kaj Olsen whose telephone number is (571) 272-1344. The examiner can normally be reached on Monday through Friday from 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AU 1753
April 30, 2007



KAJ K. OLSEN
PRIMARY EXAMINER